ACUTE TOXICITY SUMMARY

HYDROGEN CHLORIDE

(hydrogen chloride, anhydrous hydrogen chloride, muriatic acid)

CAS Registry Number: 7647-01-1

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**2,100 μg/m³**
Critical effect(s)	upper respiratory symptoms
Hazard Index target(s)	Respiratory System; Eyes

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	colorless gas
Molecular formula	HCl
Molecular weight	36.46
Density	1.49 g/L @ 25°C
Boiling point	-84.9°C
Melting point	-114.8°C
Flashpoint	not applicable
Explosive limits	unknown
Solubility	soluble in water, alcohol, benzene, ether; insoluble in hydrocarbons
Odor threshold	0.26-10.0 ppm (AIHA, 1989a)
Odor description	sharp, irritating (AIHA, 1989a)
Metabolites	not applicable
Conversion factor	1 ppm = 1.49 mg/m³ @ 25°C

III. Major Uses or Sources

Hydrogen chloride (HCl) is used in the manufacture of vinyl chloride, fertilizers, dyes, artificial silk, and pigments for paints. It is also used in electroplating, soap refining, and leather tanning. Other consumers of HCl include the photographic, textile and rubber industries (HSDB, 1994). Hydrogen chloride is produced in large quantities during combustion of most materials and especially chlorine-containing materials. Thus, HCl is a major product formed during the thermal decomposition of polyvinyl chloride, a commonly used plastic polymer (Burleigh-Flayer *et al.*, 1985). It is also released in large quantities during the test firing of some rocket and missile engines (Wohlslagel *et al.*, 1976).

IV. Acute Toxicity to Humans

Inhalation exposure to high concentrations of HCl fumes may result in coughing, choking sensation, burning of the respiratory tract, and pulmonary edema (Proctor *et al*., 1991). Dental erosion has been reported in workers chronically exposed to low levels of gaseous hydrogen chloride (Finkel, 1983). Reactive Airway Dysfunction Syndrome (RADS; acute, irritant-induced asthma) was reported in three male police officers (36-45 years old) who responded to a roadside chemical spill (Promisloff *et al*., 1990). Other reports of RADS include individual occupational cases (Boulet, 1988; Turlo and Broder, 1989).

Young adult asthmatic subjects (18-25 years, 5 of each sex) were exposed by a half-face mask to filtered air, 0.8 ppm HCl, and 1.8 ppm HCl during three separate 45-minute exposures (Stevens *et al*., 1992). The exposure protocol included two 15-minute exercise periods separated by a 15-minute rest period. Tests of pulmonary function included forced expiratory volume in 1 second, forced expiratory volume, maximal flow at 50% and 75% of expired vital capacity, and total respiratory resistance and peak flow. Nasal work of breathing was also measured pre- and post exposure. No significant changes in these parameters were observed following exposure to HCl at 0.8 or 1.8 ppm. There was no exposure-related increases in severity of upper respiratory, lower respiratory, or other symptoms reported by participants. Because exposure occurred by half-face mask, effects on the ocular mucosae were not addressed.

Predisposing Conditions for HCl Toxicity

Medical: Persons with preexisting skin, eye, gastrointestinal tract (including ulcers) or respiratory conditions or underlying cardiopulmonary disease may be more sensitive to the effects of HCl exposure (Reprotext, 1999).

Chemical: Persons also exposed to formaldehyde might be at increased risk for developing cancer (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

A single baboon exposed for 5-minutes to 16,570 ppm (24,690 mg/m^3) HCl was dyspneic until death 18 days following exposure (Kaplan *et al*., 1985). Pneumonia, pulmonary edema, tracheitis, and epithelial erosion were noted at autopsy. Baboons exposed for 15-minutes to 500, 5,000 or 10,000 ppm (750, 7,500, or 15,000 mg/m^3) HCl exhibited a concentration-related increase in respiratory rate and minute volume (Kaplan *et al*., 1988). A marked decrease in arterial blood oxygenation was observed in baboons exposed to 5,000 or 10,000 ppm. Pulmonary function parameters measured 3 days and 3 months following exposure were not significantly different from pre-exposure measurements. However, the animals were anesthetized with Ketamine which could reduce airway resistance and bronchospasm (Bovill *et al., 1*971). Histopathologic examination performed 12 months post-exposure (Kaplan *et al., 1*993a) found pulmonary hemorrhage, edema, fibrosis, and bronchiolitis in the medial right lung of one of three animals exposed to 10,000 ppm. In another of the three animals zonal atelectasis and focal multiple

hemorrhages were observed in the right lung. In each of the three animals exposed to 5,000 ppm and examined, focal, patchy hemorrhages were observed.

A 30-minute LC_{50} in rats and mice is reported as 5,666 ppm (8,442 mg/m³) and 2,142 ppm (3,192 mg/m³) HCl aerosol, respectively (Darmer *et al*., 1974). Alveolar emphysema, atelectasis, and pulmonary edema were noted at necropsy of animals that died either during or within 7 days following exposure. Bloody nasal discharge, indicative of purulent bronchitis, was observed in animals of both species surviving the exposure.

A 1-hour LC_{50} of 2,810 ppm in rats was reported by Hartzell and colleagues (1985). Rats were exposed to concentrations of HCl ranging from 1,793-4,854 ppm HCl for one hour and the mortality following exposure was recorded over a 14-day observation period. Hartzell *et al*. also reported LC_{50s} of 15,900 ppm, 8,370 ppm, 6,920 ppm, 5,920 ppm and 3,715 ppm, for rats exposed for 5 minutes, 10 minutes, 15 minutes, 22.5 minutes, and 30 minutes, respectively.

A decrease in respiratory rate was observed in guinea pigs exposed to 320 ppm (480 mg/m³) HCl for 6-minutes and to 680 ppm (1,010 mg/m³) HCl for less than 1-minute (Burleigh-Flayer *et al*., 1985). The RD_{50} is the concentration of a chemical in air that is associated with a 50% decrease in respiratory rate, and is used as a measure of irritancy. The RD_{50} in animals has a predictable relationship to irritation in man (Kane *et al*., 1979). The RD_{50} in mice was reported as 309 ppm (460 mg/m³) for a 10-minute exposure (Kane *et al*., 1979).

In addition to respiratory irritation, HCl exerts ocular effects. Corneal opacities were observed in guinea pigs following a 30-minute exposure to HCl concentrations of 680 ppm (1,010 mg/m³; 1 of 4), 1,040 ppm (1,550 mg/m³; 4 of 6) and 1,380 ppm (5 of 5), but not 320 ppm (480 mg/m³). Cloudy corneas were also reported 90 days post-exposure by Kaplan *et al*. (1993b) in guinea pigs exposed for 15 minutes to 4,200 ppm, but not at 500 ppm (Burleigh-Flayer *et al*., 1985). Coughing, frothing at the mouth, excess salivation, and blinking and rubbing of the eyes were observed in baboons following a 5-minute exposure to 810 ppm (1,210 mg/m³) HCl (Kaplan *et al*., 1985). No signs of irritation were observed following a 5-minute exposure to 190 ppm (280 mg/m³) HCl.

In another study conducted in exercising guinea pigs (Malek and Alarie, 1989), a concentration of 107 ppm for 30 minutes was irritating and a concentration of 140 ppm was incapacitating at 16.5 minutes.

VI. Reproductive or Developmental Toxicity

The reproductive hazard of hydrogen chloride to humans is unknown (Reprotext, 1999). Few studies on the reproductive effects of HCl exposure were found in the literature. Maternal exposure to a high concentration of a strong acid could result in metabolic acidosis and subsequent fetal acidemia which has been linked with low Apgar scores, neonatal death, and seizures. However, there is no evidence linking HCl exposure to fetal acidemia (Reprotext, 1999).

Pregnant rats exposed to 300 ppm (450 mg/m³) HCl for 1 hour on the 9th day of gestation exhibited signs of severe dyspnea and cyanosis (Pavlova, 1976; 1978). The exposure was lethal to one-third of the exposed rats (number of rats exposed not reported). Increased mortality was also observed in the progeny of the exposed rats compared to that of controls. The author implies that organ functional abnormalities in the progeny resulted from *in utero* exposure. However, the lack of key experimental details and the ambiguity of organ function tests make this conclusion difficult to validate.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 1.4 ppm (2,100 μg/m³)

Study	Stevens *et al*., 1992
Study population	10 asthmatics aged 18-25
Exposure method	inhalation via half face mask to 0.8 or 1.8 ppm HCl
Critical effects	upper respiratory system symptoms of sore throat; nasal discharge
LOAEL	not observed
NOAEL	1.8 ppm
Exposure duration	45 minutes
Extrapolated 1 hour concentration	1.4 ppm (1.8^1 ppm* 0.75 h = C^1 * 1 h) (see Table 12 for information on "n")
LOAEL uncertainty factor	1
Interspecies uncertainty factor	1
Intraspecies uncertainty factor	1
Cumulative uncertainty factor	1
Reference Exposure Level	1.4 ppm (2.1 mg/m³; 2,100 μg/m³)

No significant effects on pulmonary function (forced expiratory volume in one second, forced expiratory volume, maximal flow at 50% and 75% of expired vital capacity, and total respiratory resistance and peak flow) or nasal work of breathing were observed in asthmatics aged 18-25 years exposed via half-face mask to 0.8 or 1.8 ppm HCl for 45 minutes, including 30 minutes of exercise. Additionally, there was no association between HCl exposure and upper respiratory symptoms of sore throat and nasal discharge. There was no association between HCl exposure and lower respiratory symptoms of cough, chest pain, burning, dyspnea and wheezing. The lack of effects on the pulmonary functions measured is not surprising because of the extreme water-solubility of HCl. The high water solubility of HCl supports upper airway effects as the most sensitive target endpoint since the HCl would dissolve there. While the animal studies summarized in this document suggest that HCl does penetrate and affect the lower respiratory system, this would be expected to occur mostly at higher concentrations of HCl.

Level Protective Against Severe Adverse Effects

The RD_{50} in mice for a 10-minute exposure to HCl is reported as 309 ppm (460 mg/m³). NRC applied an uncertainty factor of 10 to the RD_{50} to account for interspecies differences yielding a 1-hour EEGL of 31 ppm. The EEGL was further reduced to 20 ppm (29.8 mg/m³) because "of the paucity of human data."

A 1-hour SPEGL (Short-term Public Emergency Planning Level) of 1 ppm is also recommended by NRC. The rationale states "...in connection with community exposure during space shuttle launches, the Committee recommends lower concentrations, to avoid adverse effects that might occur in a more sensitive population..." (NRC, 1987). While it appears that no supporting data are cited to justify the value, the SPEGL essentially incorporates an additional 20-fold safety factor to protect sensitive subpopulations and is an excessively low value, lower than the acute REL recommended to protect against mild adverse effects. However, since the development of the SPEGL, that relied largely on expert judgment since the database was poor (NRC, 1987), the Stevens *et al*. (1992) human study has become available, in addition to a number of additional animal studies. For this reason, we recommend the EEGL of 20 ppm as a level protective against severe adverse effects. The levels should be reevaluated when more data become available.

Level Protective Against Life-threatening Effects

Groups of 6 rats were exposed to the following concentrations of HCl for a single 1-hour period: 1,793, 2,281, 2,600, 4,277, 4,460, and 4,854 ppm (Hartzell *et al*., 1985). Mortality during and up to 14 days following exposure was reported.

Rat Mortality Data from Hartzell *et al*., 1985

HCl Concentration (ppm)	1,793	2,281	2,600	4,277	4,460	4,854
Mortality	0/6	3/6	1/6	7/8	6/6	6/6

The rat study was chosen since it was considered to be of greatest quality based on the number of doses and time points tested. Furthermore, Kaplan *et al*. (1987 and 1993b) suggest fairly similar lethality responses between baboons and rats for HCl exposure. A benchmark dose approach was employed using a log-normal probit analysis (Crump, 1983) of 60-minute lethality data from Hartzell *et al*. (1985). The concentration associated with a 5% incidence of lethality (ED_{05}) was 1,772 ppm; the lower 95% confidence limit (LCL) on this concentration [the BC_{05}] was 1,271 ppm. A total uncertainty factor of 30 was applied to the BC_{05} of 1,271 ppm to account for interspecies variability (3) and individual variation (10) in response.

$$\text{level protective against life-threatening effects} = BC_{05}/(UF)$$

The final level protective against life-threatening effects for HCl is therefore 42 ppm (63 mg/m³). The maximum likelihood estimates (MLE) and 95% lower confidence limits (LCL) for the 1% and 5% response rates are compared below. Refer to section IX of this toxicity summary for the graphic representation of benchmark dose derivation.

Comparison of benchmark calculations (1% vs 5%)

Response rate	MLE (ppm)	95% LCL (ppm)
1%	1,464	946
5%	1,772	1,271

VIII. References

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